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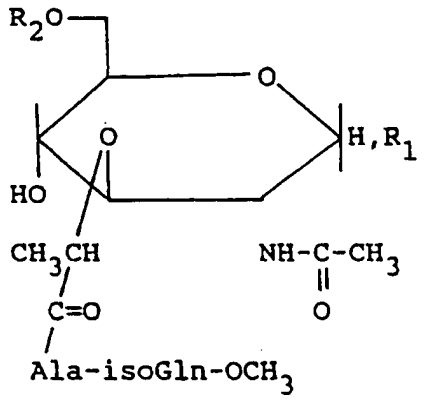
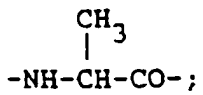
(54) Muramyl peptide derivatives and immunoregulating compositions containing them.

(57) Muramyl peptide derivatives of the formula :



(I)

wherein "Ala" is



"isoGln" is

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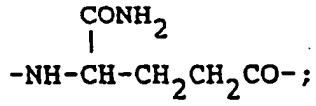
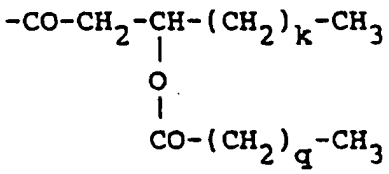
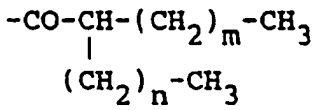


R^1 is R_3O- or R_3S-[R_3 is



(k is an integer from 8 to 12; q is an integer from 10 to 22) or R_3 is



(m is an integer from 11 to 17; n is an integer from 11 to 17)]; and R_2 is hydrogen atom or $-CO-(CH_2)_p-CH_3$ (p is an integer from 8 to 22);
which act on in vivo immunomechanism of human beings and livestock (in particular cells relevant immue responses) and are useful as immunoregulating agents.

Muramyl peptide derivatives and immunoregulating compositions containing them

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention relates to novel muramyl peptide derivatives. The muramyl peptide derivatives of the present invention acts on in vivo immunomechanism of human beings and livestock (in particular cells relevant to immune responses) and are useful as immunoregulating agents.

2. Description of the Prior Art

Muramyl peptides are known to possess various biological activities. That is, they possess in vitro activities such as;

(1) the action on cells related to immune responses (for example, monocytes or macrophages, B cells, T cells, natural killer (NK) cells and the like),

(2) the action on cells other than those mentioned above (for example, platelets, endothelial cells, fibroblasts and the like), and

(3) the action which activates complement systems.

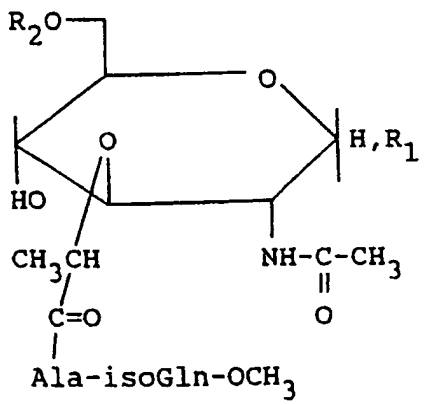
Further they show in vivo activities such as (1) immunoregulating action, and (2) enhancement of natural resistance [see Saishin Igaku, 43, No. 6, pp. 1268-1276 (1988) in Japan].

Known muramyl peptide derivatives are, for example, B30-muramyl dipeptide [Kusumoto et al; Tetrahedron letters, 49 pp. 4899-4902(1978)], muramyl dipetide-lysine [Matsumoto et al, Immunostimulants, pp. 79-97 (1987)] and those discribed in Japanese Published Unexamined Patent Application Nos. 172399/1983, 20297/1984 and 275299/1986.

However, it is still desired to develop compounds other than the known muramyl dipeptide derivatives which have more excellent activity and less toxicity.

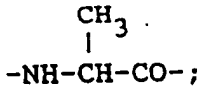
SUMMARY OF THE INVENTION

According to the present invention, a muramyl dipeptide derivative is provided, which is represented with the following formula (I):

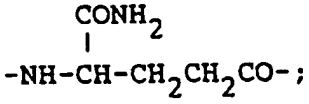


(I)

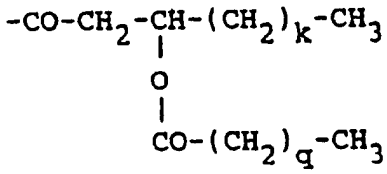
wherein "Ala" is



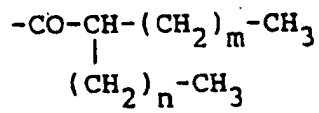
"isoGln" is



R_1 is R_3O- or R_3S- [R_3 is



(k is an integer from 8 to 12; q is an integer from 10 to 22) or R_3 is



(m is an integer from 11 to 17; n is an integer from 11 to 17)]; and R_2 is a hydrogen atom or-$CO-(CH_2)_p-CH_3$ (p is an integer from 8 to 22).

The present invention also provides an immunoregulating composition comprising a compound of the formula (I) and a pharmaceutically acceptable carrier.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

In the formula (I), examples of the groups R_3 in the group $-OR_3$ or $-SR_3$ include 3-dodecanoyloxydodecanoyl, 3-tridecanoyloxydodecanoyl, 3-tetradecanoyloxydodecanoyl, 3-pentadecanoyloxydodecanoyl, 3-hexadecanoyloxydodecanoyl, 3-heptadecanoyloxydodecanoyl, 3- octadecanoyloxydodecanoyl, 3-nonadecanoyloxydodecanoyl, 3-eicosanoyloxydodecanoyl, 3-docosanoyloxydodecanoyl, 3-heneicosanoyloxydodecanoyl, 3-tricosanoyloxydodecanoyl, 3-tetracosanoyloxydodecanoyl, 3-dodecanoyloxytridecanoyl, 3-tridecanoyloxytridecanoyl, 3-tetradecanoyloxytridecanoyl, 3-pentadecanoyloxytridecanoyl, 3-hexadecanoyloxytridecanoyl, 3-heptadecanoyloxytridecanoyl, 3-octadecanoyloxytridecanoyl, 3-nonadecanoyloxytridecanoyl, 3-eicosanoyloxytridecanoyl, 3-docosanoyloxytridecanoyl, 3-heneicosanoyloxytridecanoyl, 3-tricosanoyloxytridecanoyl, 3-tetracosanoyloxytridecanoyl, 3-dodecanoyloxytetradecanoyl, 3-tridecanoyloxytetradecanoyl, 3-tetradecanoyloxytetradecanoyl, 3-pentadecanoyloxytetradecanoyl, 3-hexadecanoyloxytetradecanoyl, 3-heptadecanoyloxytetradecanoyl, 3-octadecanoyloxytetradecanoyl, 3-nonadecanoyloxytetradecanoyl, 3-eicosanoyloxytetradecanoyl, 3-docosanoyloxytetradecanoyl, 3-heneicosanoyloxytetradecanoyl, 3-tricosanoyloxytetradecanoyl, 3-tetracosanoyloxytetradecanoyl, 3-dodecanoyloxypentadecanoyl, 3-tridecanoyloxypentadecanoyl, 3-tetradecanoyloxypentadecanoyl, 3-pentadecanoyloxypentadecanoyl, 3-hexadecanoyloxypentadecanoyl, 3-heptadecanoyloxypentadedanoyl, 3-octadecanoyloxypentadecanoyl, 3-nonadecanoyloxypentadecanoyl, 3-eicosanoyloxypentadecanoyl, 3-docosanoy loxypentadecanoyl, 3-heneicosanoyloxypentadecanoyl, 3-tricosnoyloxypentadecanoyl, 3-tetracosanoyloxypentadecanoyl, 3-dodecanoyloxyhexadecanoyl, 3-tridecanoyloxyhexadecanoyl, 3-tetradecanoyloxyhexadecanoyl, 3-pentadecanoyloxyhexadecanoyl, 3-hexadecanoyloxyhexadecanoyl, 3-heptadecanoyloxyhexadecanoyl, 3-octadecanoyloxyhexadecanoyl, 3-nonadecanoyloxyhexadecanoyl, 3-eicosanoyloxyhexadecanoyl, 3-docosanoyloxyhexadecanoyl, 3-heneicosanoyloxyhexadecanoyl, 3-tricosanoyloxyhex-

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Preferred groups of R_3 are 3-tetradecanoyloxytetradecanoyl, 3-hexadecanoyloxytetradecanoyl, 3-octadecanoyloxytetradecanoyl, 3-tetracosanoyloxytetradecanoyl and 2-tetradecylhexadecanoyl groups.

Examples of R_2 include hydrogen atom, decanoyl, undecanoyl, dodecanoyl, tridecanoyl, tetradecanoyl, pentadecanoyl, hexadecanoyl, heptadecanoyl, octadecanoyl, nonadecanoyl, eicosanoyl, docosanoyl, heneicosanoyl, tricosanoyl and tetracosanoyl groups.

R_2 is preferably hydrogen atom or tetradecanoyl group.

Preferably, "Ala" is an L-alanine residue, and "isoGln" is a residue derivated from D-isoglutamine.

The compounds of the formula (I) of the present invention are basically muramyl dipeptide derivatives, in which the muramyl dipeptide moiety has preferably the same steric configuration as that of the muramyl dipeptide moiety in natural muramyl dipeptides. Namely, the moieties of muraminic acid and dipeptide in the present muramyl dipeptides have D-steric configuration and L-alanine-D-isoglutamine configuration, respectively. However, the muramyl dipeptides of the present invention may be those having other possible steric configurations.

The group $-OR_3$ or $-SR_3$ in the definition of the formula (I) preferably combines with the saccharide moiety in the form of α-bond and β-bond, respectively.

The acyloxyacyl group in R_3 has an asymmetric carbon atom and may be in the form of D- or L-isomer, or racemic mixture.

Interesting compounds belonging to the formula (I) in the present invention include:

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetradecanolyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
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N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
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N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-d-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucpyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-(2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methyester
N-[2-0-(2-Acetamido-2,3-dideoxy-6-0-hyxadecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methyester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-dodecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-dodecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxytetradecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxytetradecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxytetradecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxytetradecnaoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-dodecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-dodecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxytetradecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxytetradecanoyl)-6-0-hexadecanoyl-1-thio-β- D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxytetradecanoyl-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-dodecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1- 0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2;3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-(2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]- L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-eicosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-eicosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eeicosanoyloxytetradecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxytetradecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxytetrdecanoyl)-6-0-octadecanoyl-α-D-gluco pyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-6-0-tetradecanoyl1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxytetradecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-1-actoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-docosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxytetradecanoyl)-6-0-decanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxytetradecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxytetradecanoyl-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxytetradecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos- 3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-6-0-dodecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxytetradecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetracosanoyloxytetradecaoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyltetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-dodecyltetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-dodecyltetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyltetradecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyltetradecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyltetradecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyltetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-dodecyltetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-dodecyltetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyltetradecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyltetradecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyltetradecanoyl)-6-0-octadecanoyl-1-thio-β-D-gluco pyranos-3-yl)-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-hexadecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-hexadecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-hexadecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-hexadecyloctadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-(2-hexadecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-hexadecyloctadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-hexadecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-hexadecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-hexadecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-hexadecyloctadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-(2-hexadecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-hexadecyloctadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-octadecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-octadecyleisocanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-octadecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-octadecyleicosanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-(2-octadecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-(2-octadecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-octadecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-octadecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-octadecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-octadecyleicosanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-(2-octadecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-(2-octadecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl] L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-dodecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-dodecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecylhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecylhexadecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecylhexadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-dodecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-dodecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecylhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecylhexadecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecylhexadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-dodecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L- alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-dodecyloctadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyloctadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyloctadecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyloctadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-dodecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-docanoyl-1-S-(2-dodecyloctadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyloctadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyloctadecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyloctadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-dodecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl- D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-(2-dodecyleicosanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyleicosanoyl)-6-0-tetradecnaoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyleicosanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-dodecyleicosanoyl)-6-0-octadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-dodecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-(2-dodecyleicosanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyleicosanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyleicosanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-(2-dodecyleicosanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-docanoyl-1-0-((3R)-3-dodecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-dodecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxydodecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxydodecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-docanoyl-1-S-((3R)-3-dodecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-dodecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxydodecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxydodecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetradecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetadecanoyloxydodecanoyl)-α-D-glucopyranos-3- yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetradecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-((3R)-3-ttradecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-tetradecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetradecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl- 1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetradecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-hexadecanoyloxydodecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-hexadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl1-0-((3R)-3-hexadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxydodecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxydodecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido 2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-octadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-octadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-octadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-octadecanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-octadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-octadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-octadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-octadecanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-eicosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-eicosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxydodecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxydodecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-eicosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-eicosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl)-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxydodecanoly)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxydodecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxydodecanol)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl- 1-0-((3R)-3-docosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxydodecanoyl)-6-0-dodecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine-methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxydodecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxydodecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1- S-((3R)-3-docosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxydodecanoyl)-6-0-dodecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxydodecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxydodecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

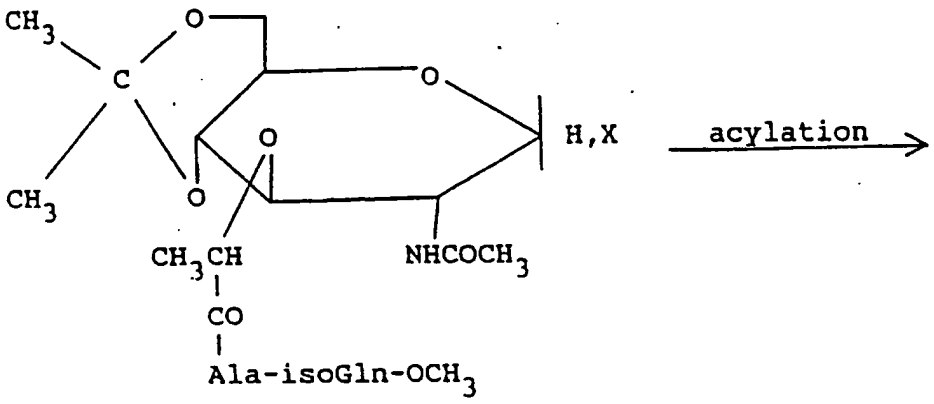
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetracosanoyloxydodecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetracosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl- 1-S-((3R)-3-tetracosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxydodecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-tetracosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetracosanoyloxydodecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-dodecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-dodecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3- dodecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxyhexadecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-dodecanoyloxyhexadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-dodecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-dodecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β- D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxyhexadecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-dodecanoyloxyhexadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-Isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl- 1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetradecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-((3R)-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl- 1-S-((3R)-3-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetradecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl- 1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxyhexadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxyhexadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-octadecanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-octadecanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-eicosanoyloxyhexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

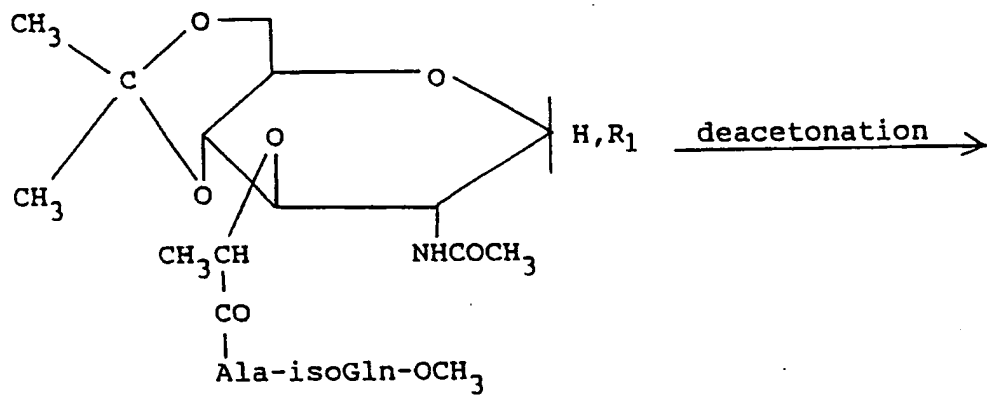
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-eicosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-eicosanoyloxyhexadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-dodecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-hexadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-dodecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-hexadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-docosanoyloxyhexadecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetracosanoyloxyhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-dodecanoyl-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-6-0-tetradecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-hexadecanoyl-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester and
N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetracosanoyloxyhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester.

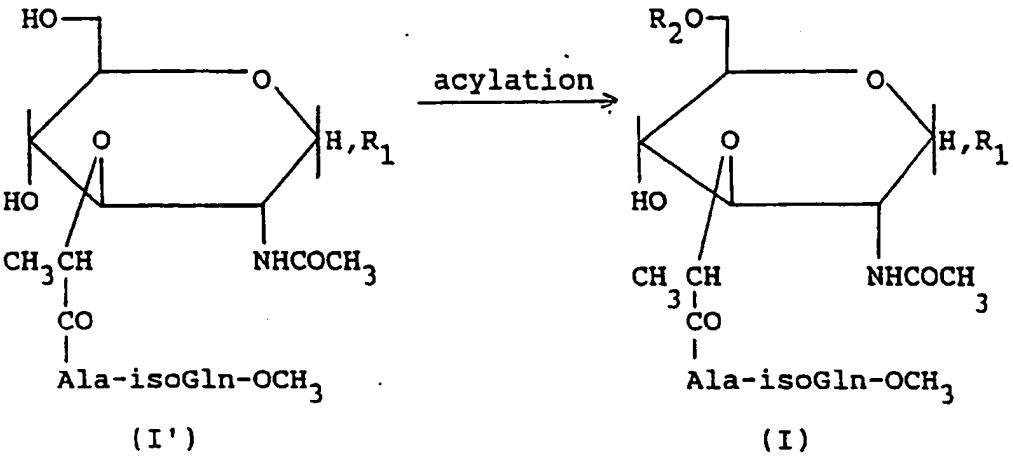
The compounds of the present invention can be basically prepared by the following process.



(II)



(III)



(I') (I)

In the formulae, X is OH or SH; R_1 and R_2 are defined as above.

The above mentioned process consists of two acylation steps (the acylations at 6th and lst positions of the glucopyranose moiety) and one deacetonation step.

The two acylation steps can be conducted by reacting a compound of the formula (II) or (I') with a specific acylating agent (R_2H, R_3H or its reactive derivative). These steps are generally carried out in an anhydrous organic solvent (for example, dimethylformamide or dioxane) and at room temperature or a slightly elevated temperature. When R_2H or R_3H (a free acid) is used, it is conducted in the presence of an appropriate condensing agent (for example, dicyclohexylcarbodiimide, N-cyclohexyl-N'-morpholinoethylcarbodiimide, N-cyclohexyl-N'-(4-diethylaminocyclohexyl)-carbodiimide or N,N'-diethylcarbodiimide). Examples of reactive derivatives of R_2H or R_3H are conventional reactive derivatives used in acylation, such as mixed acid anhydrides, active esters, acid halides and the like. The deacetonating step can be readily conducted under an acid hydrolysis condition (e.g., using 80% acetic acid aqueous solution) at a slightly elevated temperature.

The compounds of the formula (II) are known or can be readily prepared by known methods.

The compounds obtained by the above process may be purified by a conventional method such as a column chromatography using almina or silica gel, recrystallization and the like.

The compounds of the formula (I) of the present invention have an action for enhancing function of cells relevant to in vivo immune response and an action for increasing the number of said cells, and hence they are useful as an immunoregulating agent. The immunoregulating agent of the present invention can be used to enhance in vivo activities of vaccines such as BCG vaccine, hepatitis vaccine, influenza virus vaccine or the like, various antibacterial agents or anti-tumor agents.

The immunoregulating composition of the present invention comprises a compound of the formula (I) and a pharmaceutically acceptable carrier. The composition may be any dosage form for oral and parenteral administrations.

The compositions for oral administration are generally dosage forms such as powders, tablets, emulsions,capsules, granules and liquid prepartions (including liquid extracts, syrups and the like).

Examples of carriers for powders or other orally administrable solid preparations include lactose, starch, dextrin, calcium phosphate, calcium carbonate, synthetic or natural aluminium silicate, magnesium oxide, dried aluminium hydroxide, magnesium stearate, sodium bicarbonate, dried yeast and the like, and those for liquid preparations include water, glycerine, propylene glycol, simple syrup, ethanol, fatty oil, ethylene glycol, polyethylene glycol, sorbitol and the like. A typical example of the composition for parenteral administration is an injection. Liquid carriers for the injection include sterile distilled water. When a compound of the formula (I) is less soluble in water, an appropriate solubilizer is used. Each of the above preparations can be prepared by conventional methods.

When the compounds of the formula (II) of the present invention are used for enhancement of antitumor agents, they may be orally or parenterally administered to an adult human in an amount of 150 to 250μg/day in one dose. When used for enhancement of vaccines, they may be administered to an adult human in an amount of 0.5 to 2.0mg/1 to 2 weeks in one dose. For treatment of hepatitis, they may be orally or parenterally administered to an adult human 1 to 3 times for 3 months in an amount of 0.5 to 2.0mg in one dose. For enhancement of antibacterial agents, they may be used to an adult human in an

amount 20 to 100μg/day in one dose.

The immunoregulating agents of the present invention may be generally used by formulating themselves only as described above. But they may be formulated together with an agent to be enhanced its action.

Further, the immunoregulating agents of the present invention can be used for not only humans but also other mammals such as pigs, bovines, sheeps, dogs, and cats.

The present invention is illustrated with following examples.

Example 1

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 2-tetradecylhexadecanoyloxy group (279.4mg, 0.281mmol) was dissolved in 80% acetic acid aqueous solution (8ml) and the resultant was allowed to stand for 2 hours at 45° C. After confirming the completion of the reaction with T.L.C.(CH_2Cl_2 : MeOH = 10 : 1), the resultant was concentrated under reduced pressure to obtain quantitatively the title compound (266.2mg).

mp : 147.0-148.0° C

$[\alpha]_D^{25}$: +44.38° (c = 1.050, CH_2Cl : MeOH = 1 : 1)

IR γmax(KBr)cm^{-1} : 3350, 2930, 2850, 1740, 1650, 1520

NMR(CD_3OD-$CHCl_3$)δ(ppm) : 0.88(t,6H,J = 6.6Hz), 1.26(s,48H), 1.38-1.43(m,6H), 1.51-1.62(m,4H), 1.93(s,3H), 3.70(s,3H), 6.16(d,1H,J = 4.0Hz)

Example 2

N-{2-0-[2-Acetamido-2,3-dideoxy-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl]-D-lactoyl}-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 2-tetradecylhexadecanoylthio group (133.7mg) was dissolved in 80% acetic acid aqueous solution (15ml), which was allowed to react for 2 hours at 45° C. After confirming the completion of the reaction with T.L.C., the resultant was concentrated under reduced pressure and crystallized from ether to obtain quantitatively the title compound (127.0mg, crystals).

mp : 130.0-131.0° C

$[\alpha]_D^{25}$: +46.79° (c = 1,201, CH_2Cl_2 : MeOH = 1 : 1)

IRγ max(KBr)cm^{-1} : 3300, 2920, 2850, 1720, 1630, 1530

Example 3

N-{2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-tetradecanoyloxytetradecanoyloxy group (409.1mg, 0.411mmol) was dissolved in 80% acetic acid aqueous solution (15ml) and allowed to stand for an hour at 45° C. In the same manner as that in Example 1, the title compound was quantitatively obtained (386.9mg).

mp : 133.8-134.6° C

$[\alpha]_D^{25}$: +44.74° (c = 1.180, $CHCl_3$: MeOH = 1 : 1)

IR γmax(KBr)cm^{-1} : 3700-3140, 2930, 2850, 1740, 1250, 1630, 1540

NMR($CDCl_3$)δ : 0.89(t,6H,J = 2.2Hz), 1.27(m,36H), 1.43(m,6H), 1.60(m,4H), 2.00(s,3H), 2.10-2.30(m,4H), 2.44-2.67(m,6H), 3.68(s,3H), 5.31(m,1H), 6.05(d,1H)

Example 4

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-tetradecanoyloxytetradecanoylthio group (580.1mg, 0.5808mmol) was dissolved in 80% acetic acid aqueous solution (12ml) and allowed to stand for an hour at 45° C. After confirming the completion of the raction with T.L.C. (CH_2Cl_2: MeOH = 10 : 1), the resultant was concentrated under reduced pressure. The resulting syrup was lyophilized to obtain quantitatively the title compound (555.2mg, crystals).

mp : 110-111° C

$[\alpha]_D^{25}$: +26.68° (c = 0.787, CH_2Cl_2 : MeOH = 2 : 1)

IR γmax(KBr)cm^{-1} : 3650-3130, 3300, 2940, 2860, 1740, 1650, 1550,

NMR($CDCl_3$-CD_3OD)δ : 0.88 (t,6H,J = 6.6Hz), 1.25 (m,36H), 1.35 (d,3H,J = 7.0Hz), 1.39 (d,3H,J = 7.3Hz), 1.43-1.58 (m,4H), 1.93(s,3H), 1.93-2.04 (m,2H), 2.09-2.87(m,6H), 3.71(s,3H), 4.05(t,1H,J = 10.4Hz), 4.28-4.33-(m,1H), 4.31(q,1H,J = 7.0Hz), 4.38-4.43 (m,1H), 5.12(d,1H,J = 11.0Hz) 5.17-5.26(m,1H)

Example 5

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I) wherein R_1 is 2-tetradecylhexadecanoyloxy group (143.3mg, 0.150mmol) was dissolved in a mixture of dry dioxane (1.3ml) and dry N,N-dimethylformamide (DMF, 1.3ml). To the solution were added decanoic acid (29.6mg, 0.180mmol), dicyclohexylcarbodiimide (DCC, 61.7mg, 0.300mmol) and dimethylaminopyridine (DMAP, 9.1mg, 0.075mmol), and the resultant was stirred for 14 hours at room temperature. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure. The resulting syrup was subjected to a column chromatography [Wakogel® C-200 eluted with CH_2Cl_2/MeOH ((a) 150 : 1 and (b) 20 : 1)] and the eluate eluted with the eluent (b) was concentrated under reduced pressure. The resultant syrup was subjected to a column chromatography [active alumina 90 eluted with CH_2Cl_2/MeOH ((a′) 150 : 1 and (b′) 20 : 1)], to remove DMAP and the eluate eluted with the eluent (b′) gave the title compound (121.3mg, yield: 72.6%).

mp : 116.3-117.0° C

$[\alpha]_D^{25}$: +42.56° (C = 0.726, $CHCl_3$: MeOH = 2 : 1)

IR γmax(KBr)cm^{-1} : 3650-3150, 2940, 2870, 1740, 1650, 1540

NMR($CDCl_3$)δ : 0.88(t,6H,J = 6.8Hz), 0.92(t,3H,J = 7.1Hz), 1.25(m,62H), 1.39(d,3H,J = 6.6Hz), 1.41-(d,3H,J = 6.6Hz), 1.51-1.60(m,6H), 1.90-2.23(m,2H), 1.94(s,3H), 2.33(t,2H,J-7.5Hz), 2.39-2.50(m,3H), 3.69-(s,3H), 6.18(d,1H,J = 3.7Hz)

Example 6

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 2-tetradecylhexadecanoyloxy group (139.7mg, 0.147mmol) is dissolved in a mixture of dry dioxane (2ml) and dry DMF (2ml). To the solution were added tetradecanoic acid (40.0mg, 0.176mmol), DCC(60.2mg, 0.294mmol) and DMAP(8.9mg, 0.074mmol). The resultant was stirred for 12 hours at room temperature and then treated in the same manner as that in Example 5 to obtain the title compound (105.4mg, yield: 61.7%).

mp : 116.8-117.7° C

$[\alpha]_D^{25}$: +29.22° (c = 1.054, CH_2Cl_2)

IR γmax(KBr)cm^{-1} : 3700-3100, 2940, 2860, 1740, 1660, 1540

NMR($CDCl_3$)δ : 0.88(t,9H,J = 6.4Hz), 1.25(m,7H), 1.38(d,3H, J = 6.6Hz), 1.41(d,3H, J = 7.3Hz), 1.49-1.60-

(m,6H), 1.93(s,3H), 2.03-2.21(m,2H), 2.32(t,2H,J=7.7Hz), 2.38-2.74(m,3H), 3.68(s,3H), 6.17(d,1H,J=3.7Hz)

Esample 7

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 2-tetradecylhexadecanoyloxy group (122.7mg, 0.129mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF(0.5ml). To the solution were added octadecanoic acid (44.5mg, 0.155mmol), DCC(53.7mg, 0.258mmol) and DMAP(7.9mg, 0.065mmol). The resultant was stirred for 14 hours and then treated in the same manner as that in Example 5 to obtain the title compound(119.0mg, yield: 75.6%).

mp : 118.7-120.0°C

$[\alpha]_D^{25}$: +39.45° (c=0.621, $CHCl_3$: MeOH=2 : 1)

IR γmax(KBr)cm^{-1} : 3650-3150, 2930, 2860, 1740, 1650, 1540

NMR($CDCl_3$)δ : 0.88(t,9H,J=6.6Hz), 1.25(m,78H), 1.39(d,3H,J=6.6Hz), 1.41(d,3H,J=6.6Hz), 1.49-1.60(m,6H), 1.94(s,3H), 1.90-2.26(m,2H), 2.32(t,2H,J=7.3Hz), 2.39-2.50(m,3H), 3.69(s,3H), 6.18(d,1H,J=3.7Hz)

Example 8

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 2-tetradecylhexadecanoylthio (128.4mg, 0.134mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF (1.0ml). To the solution were added decanoic acid (27.4mg, 0.161mmol), DCC(54.6mg, 0.268mmol) and DMAP(8.1mg, 0.067mmol). The resultant was stirred for 6.5 hours at room temperature. After confirming the completion of the reaciton with T.L.C. (10 : 1), the resultant was lyophilized and subjected to a column chromatography [Wakogel® C-200 eluted with CH_2Cl_2/MeOH ((a) 150 : 1 and (b) 50 : 1)]. The eluate eluted with the eluent (b) gave the title compound (99.6mg, yield: 66.8%).

mp : 98.6-99.4°C

$[\alpha]_D^{25}$: +17.69° (c=0.797, CH_2Cl_2: MeOH=2 : 1)

IR γmax(KBr)cm^{-1} : 3500-3200, 2950, 2880, 1750, 1640, 1560

NMR($CDCl_3$-CD_3OD)δ : 0.88(t,6H,J=6.6Hz), 0.92(t,3H,J=7.1Hz), 1.25(m,56H), 1.34(d,3H,J=6.6Hz), 1.40(d,3H,J=7.0Hz), 1.58-1.71(m,6H), 1.90(s,3H), 1.94-2.24(m,2H), 2.33(t,2H,J=7.5Hz), 2.42-2.52(m,3H), 3.69(s,3H), 5.11(d,1H,J=10.6Hz)

Example 9

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-(2-tetradcylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 2-tetradecylhexadecanoylthio group (125.0mg, 0.131mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF (1.0ml). To the solution were added tetradecanoic acid (35.3mg, 0.157mmol), DCC(53.1mg, 0.262mmol) and DMAP (7.9mg, 0.066mmol). The resultant was stirred for 3 hours at room temperature and then treated in the same manner as that in Example 8 to obtain the title compound (125.8mg, yield: 82.5%).

mp : 99.0-100.4°C

$[\alpha]_D^{25}$: +2.13° (c=2.16, CH_2Cl_2)

IR γmax(KBr)cm^{-1} : 3650-3200, 2930, 2860, 1740, 1650, 1550

NMR($CDCl_3$)δ : 0.85-0.95(m,9H), 1.25(m,68H), 1.36(d,3H,J=6.6Hz), 1.41(d,3H,J=7.3Hz), 1.47-1.76(m,6H), 1.88-2.32(m,2H), 1.94(s,3H), 2.35(t,2H,J=7.9Hz), 2.47-2.53(m,3H), 3.70(s,3H), 5.12(d,1H,J=10.3Hz)

Example 10

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 2-tetradecylhexadecanoylthio (122.4mg, 0.128mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF (1.0ml). To the solution were added octadecanoic acid (43.0mg, 0.145mmol), DCC(52.0mg, 0.245mmol) and DMAP (7.7mg, 0.064mmol). The resultant was stirred for 4 hours at room temperature and treated in the same manner as that in Example 8 to obtain the title compound (102.7mg, yield : 65.6%).

mp : 99.3-101.0° C

$[\alpha]_D^{25}$: +2.06° (c = 0.376, CH_2Cl_2 MeOH = 2 : 1)

IR γmax(KBr)cm^{-1} : 3600-3150, 2920, 2840, 1740, 1640, 1540

NMR($CDCl_3$-CD_3OD)δ : 0.88(t,9H,J = 6.6Hz), 1.26(m,76H), 1.35(d,3H,J = 6.6Hz), 1.40(d,3H,J = 7.3Hz), 1.58-1.61(m,6H), 1.88(s,3H), 1.92-2.26(m,2H), 2.33(t,2H,J = 7.7Hz), 2.41-2.55(m,3H), 3.69(s,3H), 4.40(q,1H), 5.10-(d,1H,J = 11.0Hz)

Example 11

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-tetradecanoyloxytetradecanoyloxy group (116.9mg, 0.121mmol) was dissolved in a mixture of dioxane (1.5ml) and dry DMF (0.5ml). To the solution were added decanoic acid (24.3mg, 0.145mmol), DCC (48.4mg, 0.242mmol) and DMAP (7.2mg, 0.161mmol). The resultant was stirred for 8 hours at room temeperature. After confirming, the completion of the reaction with T.L.C. (CH_2Cl_2 MeOH = 10 : 1), the resultant was concentrated under reduced pressure. The resulting syrup was subjected to a column chromatography [Wakogel® C-200 eluted with CH_2Cl_2/MeOH ((a) 150 : 1 and (b) 35 : 1)]. The eluate eluted with the eluent (b) gave the title compound (80.4mg, yield : 59.6%).

mp : 72.0-72.8° C

$[\alpha]_D^{25}$: +27.86° (c = 0.804, CH_2Cl_2)

IR γmax(Film)cm^{-1} : 3700-3100, 2930, 2850, 1740, 1650, 1540

NMR($CDCl_3$)δ : 0.88(t,9H,J = 6.6Hz), 1.25-1.27(m,48H), 1.43(d,3H, J = 6.6Hz), 1.45(d,3H,J = 7.0Hz), 1.61-(m,6H), 2.00(s,3H), 2.04-2.24(m,2H), 2.30(t,2H, J = 7.5Hz), 2.32-2.67(m,6H), 3.69(s,3H), 4.21(q,1H,J = 6.6Hz), 5.29(m,1H), 6.05(d,1H,J = 3.3Hz)

Example 12

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester.

The compound of the formula (I′) wherein R_1 is 3-tetradecanoyloxytetradecanoyloxy (108.6mg, 0.115mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF (0.5ml). To the solution were added tetradecanoic acid (30.1mg, 0.137mmol), DCC(45.3mg, 0.228mmol) and DMAP (6.7mg, 0.057mmol). The mixture was allowed to react for 14 hours at room temperature. The resultant was treated in the same manner as that in Example 11 to obtain the title compound (99.1mg, yield: 74.6%).

mp : 72.5-73.6° C

$[\alpha]_D^{25}$: +26.51° (c = 1.388,CH_2Cl_2)

IR γmax(film)cm^{-1} : 3700-3150, 2930, 2850, 1740, 1660, 1540

NMR($CDCl_3$)δ : 0.88(t,9H,J = 6.6Hz), 1.25-1.38(m,56H), 1.43(d,3H,J = 6.6Hz), 1.45(d,3H,J = 7.0Hz), 1.60-(m,6H), 1.99(s,3H), 2.06-2.24(m,2H), 2.30(t,2H,J = 7.5Hz), 2.32-2.66(m,6H), 3.69(s,3H), 4.21(q,1H,J = 7.0Hz), 5.30(m,1H), 6.05(d,1H,J = 3.3Hz)

Example 13

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 3-tetradecanoyloxytetradecanoyl group (108.8mg, 0.114mmol) was dissolved in a mixture of dry dioxane (1.5ml) and dry DMF (0.5ml). To the solution were added octadecanoic acid (37.6mg, 0.137mmol), DCC (45.4mg, 0.228mmol) and DMAP (6.7mg, 0.057mmol). The resultant was stirred for 14 hours at room temperature and then treated in the same manner as that in Example 11 to obtain the title compound (95.6mg, yield: 68.5%).

mp : 68.1-69.0° C

$[\alpha]_D^{25}$: +26.15° (c = 1.338, CH_2Cl_2)

IR γmax(film)cm^{-1} : 3700-3150, 2930, 2850, 1740, 1650, 1540

NMR($CDCl_3$)δ : 0.88(t,9H,J = 6.6Hz), 1.25-1.39(m,64H), 1.43(d,3H,J = 6.6Hz), 1.44(d,3H,J = 7.0Hz), 1.58-1.60-(m,6H), 1.99(s,3H), 2.02-2.22(m,2H), 2.30(t,2H,J = 7.5Hz), 2.32-2.67(m,6H), 3.69(s,3H), 4.21(q,1H,J = 6.6Hz), 5.30(m,1H), 6.05(d,1H,J = 3.3Hz)

Example 14

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-R-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I) wherein R_1 is 3-tetradecanoyloxytetradecanoylthio (239.2mg, 0.250mmol) was dissolved in a mixture of dry dioxane (0.5ml) and dry DMF (0.5ml). To the solution were added decanoic acid (51.6ml, 0.300mmol), DCC (102.9mg, 0.50mmol) and DMAP (15.2mg, 0.499mmol), and the resultant was stirred for 2 hours at room temperature. After confirming the completion of the reaction with T.L.C. (CH_2Cl_2 MeOH = 10 : 1), DC urea of a reaction by-product was filtered off and washed with dioxane. The filtrate and washings were combined and then lyophilized. The amorphous material thus obtained was subjected to a column chromatography [Wakogel® C-200 eluted with CH_2Cl_2/MeOH ((a) 200 : 1, (b) 70 : 1, (c) 60 : 1 and (d) 40 : 1)]. The eluate eluted with the eluent (c) gave the title compound (111.6mg, yield: 40.2%).

mp : 138.6 - 139.9° C

$[\alpha]_D^{25}$: +17.09° (c = 0.702, CH_2Cl_2 : MeOH = 2:1)

IR-γmax(film)cm^{-1} : 3650-3020, 3250, 2930, 2850, 1740, 1660, 1540

NMR($CDCl_3$)δ: 0.87(t,9H,J = 5.7Hz), 1.25(m,52H), 1.39(d,3H,J = 6.6Hz), 1.58(m,6H), 1.95(s,3H), 2.10-2.28-(m,2H), 2.34(6,2H,J = 7.7Hz), 2.47-2.91(m,6H), 3.69(s,3H), 5.13(d,1H,J = 11.0Hz), 5.11-5.21(m,1H)

Example 15

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 3-tetradecanoyloxytetradecanoylthio (206.5mg, 0.215 mmol) was dissolved in dry dioxane (0.5ml) and dry DMF (0.5ml). To the solution were added tetradecanoic acid (59.0mg, 0.259 mmol), DCC (88.9mg, 0.431 mmol) and DMAP (13.1mg, 9.1077 mmol). The resultant was stirred for 2.5 hours at room temperature and then treated in the same manner as that in Example 14 to obtain the title compound (95.6mg, yield: 38.0%).

mp : 136.1 - 137.7° C

$[\alpha]_D^{25}$: +17.57° (c = 0.956, CH_2Cl_2:MeOH = 2:1)

IR γmax (film)cm^{-1}: 3650-3120, 3300, 2930, 2860, 1740, 1640, 1540

NMR($CDCl_3$)δ: 0.88(t,9H,J = 6.6Hz), 1.25(m,56H), 1.39(d,3H,J = 7.0Hz), 1.42(d,3H,J = 7.0Hz), 1.57(m,6H), 1.97(s,3H), 2.01-2.28(m,2H), 2.34(t,2H,J = 7.7Hz), 3.71(s,3H), 5.13(d,1H,J = 11.0Hz), 5.11-5.23(m,1H)

Example 16

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-tetradecanoyloxytetradecanoylthio (203.2mg, 0.212 mmol) was dissolved in a mixture of dry dioxane (0.5ml) and dry DMF (0.5ml). To the solution were added octadecanoic acid (63.1mg, 0.254 mmol), DCC (87.5mg, 0.424 mmol) and DMAP (12.9mg, 0.106 mmol). The resultant was stirred for 3 hours at room temperature and then treated in the same manner as that in Example 14 to obtain the title compound (112.2mg, yield: 43.2%).
mp : 133.7 - 134.5°C
$[\alpha]_D^{25}$: +17.46° (c=1.122, CH_2Cl_2:MeOH = 2:1)
IR γmax(film)cm^{-1} : 3700-3150, 3320, 2960, 2900, 1750, 1680, 1580
NMR($CDCl_3$)δ: 0.87(6,9H,J=5.5Hz), 1.25(m,6.6H), 1.39(d,3H,J=5.9Hz), 1.57(m,6H), 1.95(s,3H), 1.95-2.18-(m,2H), 2.25-2.90(m,6H), 2.38(t,2H,J=7.1Hz), 3.69(s,3H), 5.13(d,1H,J=11.0Hz), 5.11-5.20(m,1H)

Example 17

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-hexadecanoyloxytetradecanoyloxy (408.1mg, 0.410 mmol) was dissolved in 80% acetic acid aqueous solution (15ml), which was allowed to stand for 1.5 hours at 45°C. In the same manner as that in Example 4, the title compound (391.7mg) was quantitatively obtained from the above solution.
m.p. : 134.2 - 135.5°C
$[\alpha]_D^{25}$: +47.38° (c=0.878, CH_2Cl_2:MeOH = 1:1)
IR γmax $(cm)^{-1}$: 3700-3100(OH), 3300(NH) 2920, 2850(CH) 1740(ester) 1650, 1530(amido)
NMR($CDCl_3$)δ : 0.88(t,9H,JMe$CH_2$6Hz,3MeCH_2), 1.25(m,40H,20CHz), 1.42(d,3H,J_{MeCH}7.3Hz,MeC of Ala), 1.45(d,3H,J_{MeCH}7.3Hz,HeC of Lac), 1.57-1.60(m,6H,3MeCh_2), 1.95-2.17(m,2H,CH_2CH of Gln), 2.00-(S,3H,AcN), 2.30(t,2H,J$CH_2CH_2$7.5Hz,CH_2CO of Gln), 2.37-2.66(m,6H,3CH_2CO), 3.68(S,3H,COOMe), 5.30-5.42(m,1H,H-3 of C_{17}-O-C_{16}), 6.03(d,1H,$J_{1,2}$,3.3Hz,H-1),

Example 18

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-hexadecanoyloxytetradecanoyloxy (191.1mg, 0.200mmol) was dissolved in a mixture of dry dioxane (3.0ml) and dry DMF (1.0ml). To the solution were added octadecanoic acid (74.0mg, 0.260mmol), DDC(82.5mg, 0.400mmol) and DMAP (12.2mg, 0.100mmol). The resultant was stirred for 16 hours at room temperature. In the same manner as that in Example 11, the title compound (193.1mg, yield : 78.9%) was obtained.
mp : 69.5-71.0°C
$[\alpha]_D^{25}$: +40.69° (C=1.504, CH_2Cl_2 : MeOH=2 : 1)
IR γmax(cm^{-1}): 3700-3130(OH), 3300(NH), 2930, 2860(CH), 1740(ester), 1660, 1540(amido),
NMR($CDCl_3$) : 0.88(t,9H,JMe$CH_2$6.6Hz,3MeCH_2), 1.25(m,68H,34CH_2), 1.43(d,3H,JMeCH5.9Hz,MeC of Ala), 1.45(d,3H,JMeCH5.9Hz,MeC of Lac), 1.60(m,6H,3MeCH_2), 1.99(s,3H,AcN), 2.19-2.66(m,8H,CH_2CH of Gln,3CH_2CO), 2.35(t,2H,J$CH_2CH_2$7.7Hz,CH_2CO of Gln), 3.69(s,3H,COOMe), 5.30(m,1H,H-3 of $C_{14}OC_{16}$), 6.05(d,1H,$J_{1,2}$, 2.9Hz,H-1)

Example 19

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecaonyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-hexadecanoyloxytetradecanoylthio (586.6mg, 0.580mmol) was dissolved in 80% acetic acid aqueous solution (12ml), which was allowed to stand for an hour at 45°C. In the same manner as that in Example 4, the title compound (563.4mg) was quantitatively obtained.

mp : 94.6-95.8°C

$[\alpha]_D^{25}$: +28 06(C = 1.112, CH_2Cl_2. : MeOH = 1 : 1)

IR γmax(cm^{-1}) : 3680-3130(OH), 3300(NH), 2940, 2870(CH), 1740(ester), 1650, 1550(amido)

NMR($CDCl_3$) : 0.88(t,6H,JMeCH26.4Hz,2$MeCH_2$), 1.27(m,40H,20CH_2), 1.37(d,3H,JMeCH7.0Hz,MeC of Lac), 1.41(d,3H,JMeCH7.0Hz,MeC of Ala), 1.60(m,4H,2$MeCH_2$), 1.91(s,3H,AcN), 1.91-2.02(m,1H,$CHCH_2$ of Gln), 2.21-2.90(m,6H,CH_2CO of Gln,2CH_2CO), 3.70(s,3H,COOMe), 4.05(t,1H,$J_{6a,6b}$,10.3Hz,H-6a), 4.22-4.26-(m,2H,CH of Lac and Ala), 4.34-4.39(m,1H,CH of Gln), 5.13(d,1H,$J_{1,2}$10.6Hz,H-1), 5.21-5.25(m,1H,H-3 of $C_{14}OC_{16}$)

Example 20

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I') wherein R_1 is 3-hexadecanoyloxytetradecanoylthio(340.0mg, 0.350mmol) was dissolved in a mixture of dry dioxane (4.0ml) and dry DMF(1.5ml). To the solution were added octadecanoic acid(129.4mg, 0.455mmol), DCC(144.4mg, 0.700mmol) and DMAP(21.4mg, 0.175mmol). The resultant was stirred for 3 hours at room temperature. In the same manner as that in Example 14, the title compound (203.1mg, yield : 46.8%) was obtained.

mp : 171.2-172.8°C

$[\alpha]_D^{25}$: +17.01° (C = 0.723, CH_2Cl_2 : MeOH = 2 : 1)

IR γmax(cm^{-1}) : 3320, 3270(NH, OH), 2920, 2850(CH), 1740(ester), 1650, 1540(amido)

NMR($CDCl_3$) : 0.87(t,9H,JMeCH5.3Hz,3$MeCH_2$), 1.25(m,70H,35CH_2), 1.39(d,3H,JMeCH6.6Hz,MeC of Ala), 1.58(m,6H,3$MeCH_2$), 1.94(s,3H,AcN), 2.22-2.91(m,2H,CH_2CO of Gln), 2.32(t,2H,J$CH_2CH_2$7.7Hz,CH_2CO of Gln), 3.69(s,3H,COOMe), 5.13(d,1H,$J_{1,2}$11.0Hz,H-1), 5.11-5.20(m,1H,H-3 of C_{14}-O-C_{16})

Example 21

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-octadecanoyloxytetradecanoyloxy(388.9mg, 0.380mmol) was dissolved in 80% acetic acid aqueous solution(15ml), which was allowed to stand for 2 hours at 45°C. In the same manner as that in Example 4, the title compound (373.7mg) was quantitatively obtained(373.7mg).

mp : 187-188.5°C

$[\alpha]_D^{25}$: +47.11° (C = 0.900, CH_2Cl_2 : MeOH = 1 : 1)

IR γmax(cm^{-1}) : 3700-3100(OH), 3300(NH), 2910, 2850(CH), 1740(ester), 1650, 1540(amido)

NMR($CDCl_3$) : 0.88(t,9H,JMe$_1$$CH_2$7.0Hz,3$MeCH_2$), 1.25(m,44H,22$CH_2$), 1.41(d,3H,JMeCH7.8Hz,MeC of Ala), 1.44(d,3H,JMeCH7.8Hz,MeC of Lac), 1.99(s,3H,AcN), 1.94-2.04(m,2H,CH_2CH of Gln), 2.30-(t,2H,J$CH_2CH_2$8.0$_z$,CH_2CO of Gln), 2.27-2.46(m,6H,3CH_2CO), 3.70(s,3H,COOMe), 5.30(m,1H,H-3 of $C_{14}OC_{18}$), 6.05(d,1H,$J_{1,2}$7.8Hz,H-1)

Example 22

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-octadecanoyloxytetradecanoyloxy(177.0mg, 0.18mmol) was in a mixture of dry dioxane(3.0ml) and dry DMF(1.0ml). To the solution were added octadecanoic acid(66.6mg, 0.234mmol), DCC(74.3mg, 0.360mmol) and DMAP(11.0mg, 0.090mmol). The resultant was stirred for 16 hours at room temperature. In the same manner as that in Example 11, the title compound (164.0mg, 72.8%) was obtained.

mp : 106-108.5° C

$[\alpha]_D^{25}$: +38.46° (C = 0.624, CH_2Cl_2 : MeOH = 1 : 1)

IR γmax(cm^{-1}) : 3700-3150(H), 3300(NH), 2930, 2860(CH), 1740(ester), 1660, 1540(amido)

NMR($CDCl_3$) : 0.88(t,9H,J$CH_2CH_2$6Hz,3MeCH_2), 1.25(m,72H,36CH_2), 1.43(d,3H,JMeCH6.2Hz,MeC of Lac), 1.59(m,6H,3MeCH_2), 1.99(s,3H,AcN), 2.01-2.20(m,8H,CH_2CH of Gln,3CH_2CO), 2.30-(t,2H,J$CH_2CH_2$7.7Hz,CH_2CO of Gln), 3.69(s,3H,COOMe), 5.30(m,1H,H-3 of $C_{14}OC_{18}$), 6.05(d,1H,$J_{1,2}$3.0Hz,H-1)

Example 23

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-octadecanoyloxytetradecanoylthio(634.1mg, 0.610mmol) was dissolved in 80% acetic acid acqueous solution(15ml), which was allowed to stand for an hour at 45° C. In the same manner as that in Example 4, the title compound (609.6mg) was quantitatively obtained.

mp : 112.5-113.8° C

$[\alpha]_D^{25}$: +24.62° (C = 0.600, Ch_2Cl_2 : MeOH = 1 : 1)

IR γmax(cm^{-1}) : 3400-3100(OH), 3260(NH), 2910, 2850(CH), 1740(ester), 1640, 1530(amido)

NMR($CDCl_3$) : 0.88(t,6H,JMeCH_2,4.0Hz,2MeCH_2), 1.25(m,44H,22CH_2), 1.33(d,3H,JMeCH7.3Hz,MeC of Lac), 1.36(d,3H,JMeCH7.3Hz,MeC of Ala), 1.58(m,4H,2MeCH_2), 1.92(s,3H,AcN), 1.91-2.04(m,2H,CHCH_2 of Gln), 2.26(m,6H,CH_2CO of Gln,2CH_2CO), 3.69(s,3H,COOMe), 4.02-4.09(t,1H,$J_{6a,6b}$8.7Hz,H-6a), 4.28(m,1H,CH of Gln), 5.08(d,1H,$J_{1,2}$4.0Hz,H-1), 5.21(m,1H,H-3 of C_{14}-O-C_{18})

Example 24

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl- 1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-octadecanoyloxytetradecanoylthio(400.0mg, 0.400mmol) was dissolved in a mixture of dry dioxane (4.0ml) and dry DMF(1.5ml). To the solution were added octadecanoic acid(147.9mg, 0.520mmol), DCC(165.1mg, 0.800mmol) and DMAP(24.4mg, 0.200mmol), and the resultant was stirred for 3.5 hours at room temperature. In the same manner as that in Example 14, the title compound (258.6mg, yield : 51.0%) was obtained.

mp : 123.1-124.5° C

$[\alpha]_D^{25}$: +17.01° (C = 0.723, CH_2Cl_2 : MeOH = 2 : 1)

IR γmax(cm^{-1}) : 3650-3150(OH), 3300(NH), 2930, 2850(CH), 1730(ester), 1650, 1550(amido)

NMR($CDCl_3$) : 0.88(t,9H,JMe$CH_2$5.5Hz,3MeCH_2), 1.25(m,74H,37CH_2), 1.34(d,3H,JMeCH6.6Hz,MeC of Ala), 1.44-1.67(m,6H,3MeCH_2), 1.85(s,3H,AcN), 2.17-2.79(m,2H,CH_2CHof Gln), 2.31(t,2H,JCHh$_2$$CH_2$8.4Hz,$CH_2$CO of Gln), 3.70(s,3H,COOMe), 5.10(d,1H,$J_{1,2}$10.6Hz,H-1), 5.14(m,1H,H-3 of $C_{14}OC_{18}$)

Example 25

N-[2-0-{2-Acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-tetracosanoyloxytetradecanoyloxy(465.2mg, 0.420mmol) was dissolved in 80% acetic acid aqueous solution (15ml), which was allowed to stand for an hour at 45° C. In the same manner as that in Example 4, the title compound(448.3mg) was quantitatively obtained.

mp : 183.5-185° C

$[\alpha]_D^{25}$: +34.13° (C=0.920, CH_2Cl_2 : MeOH=2 : 1)

IR γmax(cm^{-1}) : 3700-3120(OH), 3300(NH), 2930, 2850(CH), 1740(ester), 1660, 1540(amido)

NMR($CDCl_3$) : 0.89(t,9H,JMe$CH_2$6.6Hz,3MeCH_2), 1.25(m,56H,28CH_2), 1.41(d,3H,JMeCH6.9Hz,MeC of Ala), 1.44(d,3H,JMeCH6.9Hz,MeC of Lac), 1.60(m,6H,3MeCH_2), 1.99(s,3H,AcN), 1.94-2.01(m,2H,CH_2CHof Gln), 2.20-2.39(m,6H,3CH_2CO), 2.29(t,2H,J$CH_2CH_2$13Hz,CH_2OO of Gln), 3.69(s,3H,COOMe), 5.30(m,1H,H-3 of $C_{14}OC_{24}$), 6.05(d,1H,$J_{1,2}$2.9Hz,H-1)

Example 26

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherein R_1 is 3-tetracosanoyloxytetradecanoyloxy (234.8mg, 0.220mmol) was dissolved in a mixture of dry dioxane (3.0ml) and dry DMF(1.0ml). To the solution were added octadecanoic acid (81.3mg, 0.286mmol), DCC (90.8mg, 0.440mmol) and DMAP(13.4mg, 0.110mmol), and the resultant was stirred for 12 hours at room temperature. In the same manner as that in Example 11, the title compound (200.7mg, yield : 68.3%) was obtained.

mp : 66.5-68° C

$[\alpha]_D^{25}$: +34.11° (c=0.680, CH_2Cl_2 : MeOH=1 : 1)

IR γmax(cm^{-1}) : 3700-3100(OH), 3300(NH), 2930, 2850(CH), 1760(ester), 1660, 1540(amido)

NMR($CDCl_3$) : 0.88(t,9H,J$CH_2CH_2$6.6Hz,3MeCH_2), 1.25(m,88H,44CH_2), 1.43(d,3H,JMeOH6.6Hz,MeC of Ala), 1.44(d,3H,JMeOH7.0Hz,MeC of Lac), 1.61(m,6H,3MeCH_2), 2.00(m,8H,CH_2CH of Gln,3CH_2CO), 1.99-(s,3H,AcN), 2.33(t,2H,J$CH_2CH_2$4.2Hz,CH_2CO of Gln). 3.65(s,3H,COOMe), 4.20(q,1H,JMe$_1$CH,Hz,MeCH of Ala), 5.29(m,1H,H-3 of $C_{14}OC_{24}$), 6.04(d,1H,$J_{1,2}$33Hz,1-H)

Example 27

N-[2-0-{2-Acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (III) wherein R_1 is 3-tetracosanoyloxytetradecanoylthio (617.9mg, 0.550mmol) was dissolved in 80% acetic acid aqueous solution (12ml), which was allowed to stand for an hour at 45° C. In the same manner as that in Example 4, the title compound (595.9mg) was quantitatively obtained.

mp : 168.5-170.1° C

$[\alpha]_D^{25}$: +5.18° (C=0.772, CH_2Cl_2 MeOH=1 : 1)

IR γmax(cm^{-1}) : 3500-3200(OH), 3280(NH), 2910, 2850(CH), 1720(ester), 1630, 1540(amido)

NMR($CDCl_3$) : 0.88(t,6H,JMe$_1$$CH_2$ Hz,2MeCH_2) 1.25(m,56H,28CH_2), 1.30(d,3H,JMeCH8.3Hz,MeC of Lac), 1.34(d,3H,JMeCH7.5Hz,MeC of Ala), 1.58(m,4H,2MeCH_2), 1.97-1.91(m,2H,2MeCH_2), 1.94(s,3H,AcN), 2.25-(m,6H,$CHCH_2$ of Gln), 3.69(s,3H,COOMe), 4.05(t,1H,$J_{6a,6b}$10.1Hz,H-6a), 4.24-4.28(m,1H,CH of Gln), 5.09-(d,1H,$J_{1,2}$10.8Hz,H-1), 5.13-5.19(m,1H,H-3 of C_{14}-O-C_{24})

Example 28

N-[2-0-{2-Acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester

The compound of the formula (I′) wherien R_1 is 3-tetracosanoyloxytetradecanoylthio (411.8mg, 0.380mmol) was dissolved in a mixture of dry dioxane (4.0ml) and dry DMF (1.5ml). To the solution were added octadeconoic acid (140.5mg, 0.494mmol), DCC(156.8mg, 0.760mmol) and DMAP (23.2mg, 0.190mmol), and the resultant was stirred for 3 hours at room temperature. In the same manner as that in Example 14, the title compound (223.5mg, yield:43.5%) was obtained. mp : 147.5-149.0° C

$[\alpha]_D^{25}$: +17.40° (C=0.632,CH_2Cl_2 MeOH=1 : 1)

IR νmax(cm^{-1}) : 3600-3200(OH), 3300(NH), 2950, 2880(CH), 1750(ester), 1660, 1560(amido)

NMR($CDCl_3$) : 0.88(t,9H,JMeCH5.5Hz,3$MeCH_2$), 1.25(m,86H,43CH_2), 1.35(d,3H,JMeCH6.3Hz,MeC of Ala), 1.57(m,6H,3$MeCH_2$), 1.90(s,3H,AcN), 2.05-2.90(m,2H,CH_2CH of Gln), 2.35(t,2H,J$CH_2CH_2$7.8Hz,CH_2CO of Gln), 3.68(s,3H,COOMe), 5.13(d,1H,$J_{1,2}$11.0Hz,H-1), 5.15(m,1H,H-3 of $C_{14}OC_{24}$)

Pharmacological activities of the compounds of the present invention are shown as follows.

(1) Hepatitis-vaccine enhancing activity (adjuvant activity)

A compound of the present invneiton was dissolved in lipidmicrosphere (1mg/ml). On the other hand, a solution of hepatitis B virus surface antigen (HBs) in physiological saline was prepared (50μg/ml). The above solutions in equal amounts were mixed to prepare a test solution. A control solution was prepared by the exclusion of the compound of the present invention from said test solution. A mixture of a suspension of aluminium hydroxide gel in physiological saline (1mg/ml) and said hepatitis vaccine preparation in equal amounts was prepared as another control solution. The test solution (0.2ml) was intraperitoneally administered to each mouse in one group consisting of seven female CDF_1 mice.

Blood samples were collected from the fundus ocluli vein of each mouse every week after the administration and then centrifuged to obtain serums. Three weeks after the administration, 0.2ml of the test liquid was intraperitoneally administered again to each mouse for secondary stimulation. Then blood collecting was conducted every week to obtain serums after the application of the secondary stimulation, in the same manner as that described above.

The amount of the IgG antibodies against the hepatitis B virus surface antigens (HBs) in the serums thus obtained was determined with an ELISA method. The results are shown in Table 1.

Table 1

※ Adjuvant activities on heptatis β virus surface antigens - Experiment 1

Test material	Anti HBs serum antigen value (average value ± S.D.) O.D 415nm 5000-fold dilution				
	1 W	2 W	3 W	4 W	5 W
Example 1	0.001±0.001	0.018±0.000	0.074±0.002	0.815±0.011	0.843±0.005
2	0	0.023±0.000	0.076±0.001	0.975±0.008	0.930±0.004
3	0	0.027±0.001	0.064±0.003	0.631±0.006	0.692±0.009
4	0	0.073±0.001	0.111±0.007	0.848±0.009	0.935±0.022
5	0.001±0.001	0.021±0.001	0.048±0.001	0.643±0.013	0.490±0.009
6	0	0.020±0.002	0.069±0.001	0.477±0.005	0.529±0.005
7	0	0.016±0.003	0.071±0.004	0.426±0.000	0.470±0.010
8	0	0.067±0.003	0.114±0.002	0.897±0.012	0.845±0.016
9	0.014±0.002	0.092±0.003	0.149±0.001	0.681±0.012	0.702±0.006
10	0	0.061±0.002	0.114±0.003	0.778±0.024	0.878±0.009
11	0.010±0.002	0.083±0.002	0.124±0.003	0.602±0.009	0.716±0.020
12	0.007±0.003	0.109±0.002	0.111±0.001	0.608±0.021	0.695±0.021
13	0	0.081±0.003	0.126±0.003	0.635±0.011	0.742±0.016
14	0	0.071±0.000	0.104±0.003	0.784±0.022	0.846±0.024
15	0	0.085±0.002	0.129±0.001	0.788±0.008	0.905±0.020
16	0	0.079±0.004	0.103±0.004	0.850±0.008	0.903±0.021
Aluminum hydroxide gel	0	0	0	0.027±0.001	0.040±0.001
Control	0	0	0	0.097±0.006	0.123±0.001

Table 1 (continued)

※ Adjuvant activities on heptatis B virus surface antigens - Experiment 2

Test material	Anti HBs serum antigen value (average value ± S.D.) O.D 415nm 20000-fold dilution				
	1 W	2 W	3 W	4 W	5 W
Example 17	0.001±0.004	0.026±0.001	0.051±0.001	0.642±0.021	0.615±0.021
18	0	0.035±0.007	0.050±0.004	0.481±0.006	0.375±0.008
19	0	0.023±0.000	0.042±0.001	0.536±0.011	0.521±0.012
20	0.002±0.001	0.044±0.005	0.056±0.003	0.814±0.018	0.708±0.002
21	0.006±0.004	0.038±0.000	0.058±0.007	0.517±0.006	0.498±0.011
22	0.005±0.004	0.036±0.007	0.053±0.001	0.294±0.006	0.254±0.002
23	0.004±0.001	0.051±0.003	0.092±0.004	0.639±0.003	0.626±0.008
24	0.007±0.001	0.034±0.001	0.050±0.000	0.579±0.007	0.513±0.011
25	0.004±0.002	0.021±0.001	0.031±0.004	0.402±0.011	0.434±0.021
26	0.001±0.006	0.015±0.006	0.032±0.008	0.192±0.002	0.163±0.004
27	0.003±0.003	0.031±0.002	0.052±0.000	0.580±0.016	0.573±0.013
28	0.005±0.003	0.062±0.004	0.086±0.004	0.611±0.018	0.543±0.029
Aluminum hydroxide gel	0	0.002±0.002	0.006±0.004	0.196±0.003	0.227±0.001
Control	0	0.017±0.000	0.022±0.001	0.267±0.004	0.232±0.004

(2) Influenza HA vaccine enhancing activity (adjuvant activity)

A compound of the present invention was dissolved in lipidmicrosphere (1mg/ml). On the other hand, a solution of influenza HA vaccine (B/nagasaki/1/87 strain) in physiological saline was prepared (100 ccA/ml). The above solutions in equal amounts were mixed to prepare a test solution. A control solution was made by the exclusion of the compound of the present inveniton from said test liquid. A mixture of a suspension of aluminium hydroxide gel in physiological saline(1mg/ml) and said influenza HA vaccine preparation in equal amounts was prepared as another control liquid. The test solution (0.2ml) was intraperitoneally administered to each mouse in one group consisting of seven female CDF_1 mice.

Blood samples were collected from the fundus oculi vein of each mouse every week after the administration and then centrifuged to obtain serums. Three weeks after the aministration, 0.2ml of the test liquid was intraperitoneally administered again to each mouse for secondary stimulation. Then, blood collecting was conducted every week to obtain serums after the application of the secondary stimulation, in the same manner as that described above.

The amount of the IgG antibodies against the influenza HA vaccine (B/Nagasaki/1/87 strain) in the serums thus obtained was determined with an ELISA mehtod. The results are shown in Table 2.

Table 2

※ Adjuvant activities on influenza HA vaccines - Experiment 1

Test material	Anti HA serum antigen value (average value ± S.D.) O.D 415nm 5000-fold dilution				
	1 W	2 W	3 W	4 W	5 W
Example 1	0.007±0.003	0.174±0.003	0.232±0.003	1.243±0.036	1.201±0.002
2	0.003±0.001	0.172±0.004	0.420±0.005	1.447±0.029	1.418±0.035
3	0.009±0.000	0.182±0.003	0.292±0.004	1.122±0.020	1.140±0.013
4	0.004±0.001	0.215±0.001	0.381±0.004	1.204±0.012	1.150±0.016
5	0	0.091±0.002	0.377±0.001	1.037±0.027	1.068±0.004
6	0.001±0.001	0.013±0.002	0.259±0.004	1.025±0.013	1.159±0.013
7	0.001±0.001	0.112±0.003	0.286±0.001	1.039±0.010	1.128±0.026
8	0.001±0.001	0.105±0.005	0.246±0.004	1.246±0.019	1.267±0.023
9	0.019±0.002	0.168±0.005	0.392±0.006	1.342±0.005	1.329±0.026
10	0.005±0.001	0.153±0.003	0.280±0.000	1.149±0.018	1.203±0.014
11	0	0.073±0.000	0.160±0.005	1.059±0.016	1.050±0.003
12	0	0.105±0.004	0.176±0.002	1.039±0.015	1.050±0.008
13	0	0.088±0.004	0.140±0.001	0.868±0.010	0.824±0.002
14	0	0.110±0.003	0.186±0.007	0.974±0.006	0.954±0.002
15	0.007±0.000	0.119±0.005	0.218±0.006	1.249±0.013	1.262±0.017
16	0.001±0.001	0.145±0.004	0.257±0.010	1.251±0.010	1.262±0.026
Aluminum hydroxide gel	0	0	0	0.162±0.004	0.263±0.007
Control	0	0	0	0.410±0.004	0.502±0.008

Table 2 (continued)

* Adjuvant activities on influenza HA vaccines - Experiment 2

Test material	Anti HA serum antigen value (average value ± S.D.) O.D 415nm 80000-fold dilution				
	1 W	2 W	3 W	4 W	5 W
Example 17	0.010±0.002	0.122±0.006	0.191±0.001	0.611±0.017	0.696±0.014
18	0	0.052±0.004	0.075±0.001	0.370±0.005	0.360±0.001
19	0	0.125±0.003	0.187±0.001	0.872±0.002	0.936±0.006
20	0.001±0.001	0.071±0.001	0.110±0.008	0.840±0.011	0.857±0.023
21	0	0.060±0.001	0.097±0.002	0.748±0.003	0.758±0.012
22	0.001±0.004	0.065±0.001	0.100±0.003	0.411±0.009	0.492±0.002
23	0.008±0.005	0.096±0.001	0.183±0.004	0.949±0.006	1.030±0.003
24	0.006±0.001	0.085±0.005	0.113±0.007	0.771±0.003	0.791±0.004
25	0.009±0.001	0.109±0.002	0.149±0.004	0.623±0.019	0.719±0.021
26	0.004±0.003	0.038±0.001	0.054±0.001	0.208±0.001	0.206±0.002
27	0	0.110±0.003	0.161±0.003	0.751±0.004	0.805±0.008
28	0.008±0.004	0.041±0.004	0.061±0.001	0.787±0.018	0.779±0.024
Aluminum hydroxide gel	0	0	0	0.152±0.008	0.181±0.008
Control	0	0.046±0.001	0.071±0.004	0.380±0.004	0.388±0.005

(3) Activation of macrophages (an effect which inhibits the growth of tumor cells)

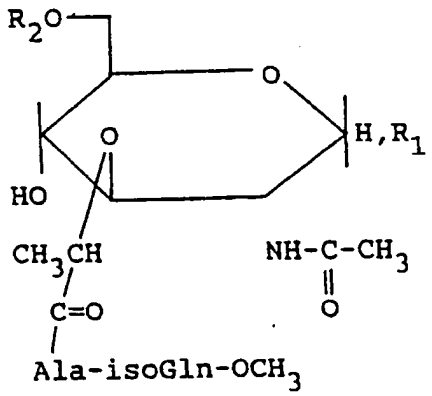
A compound of the present invention was dissolved in lipidmicrosphere to obtain a solution in a concentration of 500μg/ml, and 0.2ml of such solution was intraperitoneally administered to each mouse in one group consisting of seven female CDF_1 mice. Intraperitoneal macrophages obtained three days after the administration and L-1210 mouse leukemia cells were mixed in the ratio of cell numbers of 20 : 1, respectively. Two hundred μl of the mixture was placed in each well of one sheet of 96 well microtiter plate. After 72 hours, the increase of the cell number in each well was determined by a MTT assay method. The ratio of the cell number for the mixture of the L-1210 cells and the macrophage relative to the cell number for the L-1210 cells only(growth inhibitory ratio) was determined, and the results are shown in Table 3.

Table 3

Test material	Growth inhibitory ratio of L-1210 mouse leukemia cells(%)
Example 1	40.0
2	41.3
3	42.6
4	45.2
5	57.8
6	63.0
7	90.2
8	57.9
9	58.5
10	76.6
11	59.7
12	79.0
13	39.7
14	96.4
15	87.5
16	76.3
Control	9.1

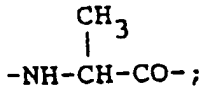
Claims

1. A muramyl dipeptide derivative of the following formula (I):

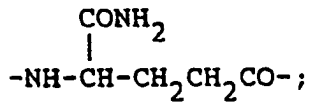


(I)

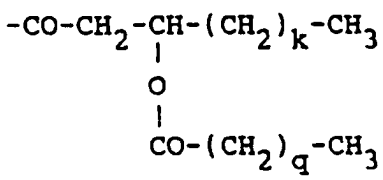
wherein "Ala" is



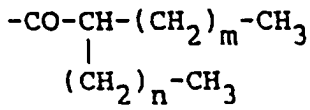
"isoGln" is



R^1 is R_3O- or R_3S-[R_3 is



(k is an integer from 8 to 12; q is an integer from 10 to 22) or R_3 is



(m is an integer from 11 to 17; n is an integer from 11 to 17)]; and R_2 is hydrogen atom or $-CO-(CH_2)_p-CH_3$ (p is an integer from 8 to 22).

2. A compound of claim 1 wherein R_3 is 2-tetradecylhexadecanoyl.
3. A compound of claim 1 wherein R_3 is (3R)-3-tetradecanoyloxytetradecanoyl.
4. A compound of claim 1 wherein R_3 is (3R)-3-hexadecanoyloxytetradecanoyl.
5. A compound of claim 1 wherein R_2 is hydrogen atom.
6. A compound of claim 1 wherein R_2 is tetradecanoyl.
7. A compound of claim 1 wherein "Ala" is L-alanine residue, and "isoGln" is D-isoglutamine residue.
8. A compound of claim 1 which is

N-[2-0-{2-acetamido-2,3-dideoxy-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-decanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-(2-tetradecylhexadecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-decanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-(2-tetradecylhexadecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-decanoyl-1-0-((3R)-3-tetradecanolyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-tetradecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-decanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-

glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-tetradecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetradecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-0-((3R)-3-hexadecanoyloxytetradecanoyl)-6-0-octadecanoyl-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-((3R)-3-hexadecanoyloxytetradecanoyl)-6-0-octadecanoyl-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-0-((3R)-3-octadecanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutmine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-octadecanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl1-0-((3R)-3-tetracosanoyloxytetradecanoyl)-α-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester,
N-[2-0-{2-acetamido-2,3-dideoxy-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester, or
N-[2-0-{2-acetamido-2,3-dideoxy-6-0-octadecanoyl-1-S-((3R)-3-tetracosanoyloxytetradecanoyl)-1-thio-β-D-glucopyranos-3-yl}-D-lactoyl]-L-alanyl-D-isoglutamine methylester.

9. An immunoregulating composition comprising a muramyl dipeptide derivative of the formula (I) as defined in claim 1 and a pharmaceutically acceptable carrier.

10. An immunoregulating composition of claim 9 in which the muramyl dipeptide derivative (I) is a compound in accordance with any one of claims 2 to 8.

11. An immunoregulating composition of claim 9 which is used for enhancing in vivo activity of a BCG, hepatitis or influenza virus vaccines.

12. An immunoregulating composition of claim 9 which is used for enhancing in vivo activity of antibacterial agents.

13. An immunoregulating composition of claim 9 which is used for enhancing in vivo activity of antitumor agents.

European Patent Office

EUROPEAN SEARCH REPORT

Application Number

EP 90 10 4006

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int. Cl.5)
Y	INFECTION AND IMMUNITY, vol. 53, no. 3, September 1986, pages 511-516, American Society for Microbiology, Washington, DC, US; M. TSUJIMOTO et al.: "Adjuvant activity of 6-O-Acyl-muramyldipeptides to enhance primary cellular and humoral immune responses in Guinea pigs: Adaptability to various vehicles and pyrogenicity" ---	1-7	C 07 K 9/00 A 61 K 39/39 A 61 K 37/02
Y	AGRIC. BIOL. CHEM., vol. 50, no. 8, 1986, pages 2091-2094, Tokyo, JP; A. HASEGAWA et al.: "Synthesis of N-(2-O-[2-acetamido-1-O-acyl (or 1,6-di-O-acyl)-2,3-dideoxy-alpha-D-gluco pyranose-3-yl]-D-lactoyl)-L-alanyl-D-iso glutamine methyl esters, and their immunoadjuvant activities" ---	1-7	
Y	INFECTION AND IMMUNITY, vol. 56, no. 1, January 1988, pages 149-155, American Society for Microbiology, Washington, DC, US; Y. KUMAZAWA et al.: "Importance of fatty acid substituents of chemically synthesized lipid A-subunit analogs in the expression of immunopharmacological activity" -----	1-7	TECHNICAL FIELDS SEARCHED (Int. Cl.5) C 07 K A 61 K

The present search report has been drawn up for all claims

Place of search	Date of completion of the search	Examiner
THE HAGUE	13-06-1990	DEFFNER C-A.E.

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

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